METHOD AND APPARATUS FOR THE MASS SPECTROMETRIC ANALYSIS OF SOLUTIONS

TECHNICAL FIELD

This invention relates to a method for the mass spectrometric analysis of chemical compounds in solution, especially when the solution is the effluent of a liquid chromatograph, which is particularly suitable for compounds which are either thermally unstable or involatile.

BACKGROUND ART

The direct mass spectrometric analysis of solutions, especially those in which the solutes are thermally unstable or involatile, has long presented difficulties. There have been a number of different approaches, as reviewed, for example, by P. J. Arpino and G. Guiochon in Analytical Chemistry, June 1979, vol. 51, p. 683A, and as discussed at the first workshop on liquid chromatography—mass spectrometry, held at Montreux in October 1981, the proceedings of which were published in Journal of Chromatography, 1982, volume 251 pps. 91–225. Amongst the many different approaches that have been used, two related techniques, known as electrohydrodynamic ionisation and electrospray ionisation, respectively, will be discussed here in greater detail because of their relevance to the present invention.

In the technique of electrohydrodynamic ionization, which is fully described by B. A. Stimpson and C. A. Evans Jnr. in Journal of Electrostatics, 1978, volume 5 p. 411, and Journal of Physical Chemistry, 1978, volume 82, p. 660, the solution is introduced into the vacuum system of the mass spectrometer through a capillary tube which is charged at high voltage relative to an extractor electrode situated immediately in front of it. This electrode is usually a thin disc with a hole in the centre, and the capillary tube is positioned concentric with the hole and so that its end is situated within the thickness of the disc. The solution to be analysed is ejected into the vacuum system through the capillary by means of a syringe, which is preferably motor driven. A high positive voltage (if positive ions are to be formed) is applied to the capillary, and the syringe plunger compressed to eject liquid into the vacuum system. If the correct conditions are employed (described below), electrohydrodynamic ionisation of the liquid will take place, and a beam of ions characteristic of the solute will be formed, which can be focussed into a conventional mass analyser. In general, it is necessary to use a solvent which has a low volatility (to ensure that the pressure in the vacuum system does not rise too high), and one which is strongly polar and has a reasonably high electrical conductivity. Glycerol with sodium iodide dissolved in it is frequently employed. These requirements are thought to be due to the fact that in electrohydrodynamic ionisation the electrical field does not actually ionise the solute molecules, but merely distorts the forces present at the surface of the liquid to such an extent that ions already present in the solution are directly emitted into the gas phase. These ions are then focussed into the mass spectrometer. Consequently it is necessary for the ions to be present in solution before it encounters the electrical field, and the process works best with with polar sample molecules dissolved in strongly polar solvents, or with a liquid metal sample. Another characteristic is that the flow rate of the solution is best kept at a very low level, so that no droplets of liquid emerge from the capillary. The sample ions are then emitted from sites round the tip of the capillary, and the shape of the capillary and its position relative to the extractor electrode have a profound effect on the efficiency of the ionization.

The electrohydrodynamic ionisation mass spectra of organic samples, obtained from glycerol and sodium iodide solvents, consist in general of peaks due to the molecular ion of the solute clustered with a variable number (between 0 and 10) of glycerol molecules and sometimes sodium ions, or in the case of negative ions, iodide ions. There is little fragmentation of the molecular ion, but the spectra are often difficult to interpret because of the formation of the complex clusters containing an unknown number of glycerol molecules. Further, the use of electrohydrodynamic ionisation sources with solvents other than glycerol and sodium iodide, although possible, is not always satisfactory because the degree of ionisation of the sample in the solution is usually lower, and more volatile solvents can give rise to problems of excessive pressure in the vacuum system due to evaporating solvent vapour. This problem can be reduced by using a nozzle skimmer system and an additional pumping stage in a similar way to that described below, but the ionisation process remains of low efficiency and for organic molecules the only really satisfactory results are obtained with glycerol solvents. Consequently the use of electrohydrodynamic ionisation for liquid chromatograpy—mass spectrometery is restricted.

In contrast with electrohydrodynamic mass spectrometery, electrospray mass spectrometery does not require glycerol and sodium iodide solvents. It is based on work by M. Dole et al, (described, for example, in Journal of Chemical Physics, 1968, volume 49, p. 2240). A solution containing the sample to be ionised is sprayed from a capillary tube into a region containing gas at approximately atmospheric pressure, towards a small orifice in a plate which leads into the vacuum system of the spectrometer. A high electrical potential is applied between the spraying capillary and the walls of the chamber containing the gas (including the plate with the small orifice). A separation device, usually a nozzle skimmer system like that described by Kantrowitz and Gray in the Review of Scientific Instruments, 1951, volume 22, p. 328, is placed between the region of atmospheric pressure and the vacuum system in order to reduce the quantity of gas flowing into the vacuum system, and to produce a better collimated molecular beam.

The principle of operation of the electrospray source is as follows. The sample to be ionised is dissolved in a solvent, preferably a fairly polar one, and the resultant solution is slowly displaced through the capillary into a region of high gas pressure and electrical field, as explained. As the jet of liquid emerges it becomes charged by the strong field, the solvent begins to evaporate and the jet breaks up into a series of small charged droplets. It was originally thought that these droplets would continue to evaporate until a point known as the Rayleigh limit was reached, where the drop would become unstable because of its increasing charge to volume ratio and break up into smaller drops, at least one of which would carry the charge. This process was thought to continue until all the solvent evaporated, leaving only neutral solvent molecules in the gas phase